REMARKS

A Request for Continued Examination under 37 C.F.R. § 1.114 hereby accompanies this Amendment and Reply.

Entry of the foregoing, re-examination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. §§ 1.111 and 1.114, are respectfully requested.

Applicants thank Examiner Gambel for the informal telephonic discussion held on March 27, 2003.

I. CLAIM STATUS AND TRAVERSAL OF RESTRICTION REQUIREMENT

As correctly stated in the Office Action Summary, claims 1-18 and 20-22 were pending in this application when last examined.

Claims 1-18 and 20 have been examined on the merits, and stand rejected.

Claims 21-22 have been withdrawn from consideration as being directed to an invention that is independent and distinct from the invention as originally claimed.

According to the Examiner, newly added claims 21-22 are drawn to agents comprising peptides and peptide derivatives, including peptides set forth in SEQ ID NOS: 3-5 in the claimed methods of treating viral encephalitis previously not claimed explicitly. The Examiner contends that claims 21-22 are drawn to agents that differ in structure and modes of actions from the anti-VLA-4/anti-alpha-4 antibodies prosecuted in the current application.

Applicants respectfully traverse this restriction of the claims for at least the following reasons.

M.P.E.P. § 803 states that an application may be properly restricted to one or more claimed inventions **only if** (1) the inventions are independent or distinct as claimed, **and** (2) there is a serious burden on the Examiner if the Restriction is not required. Thus, even if appropriate reasons exist for requiring Restriction, such a Restriction should not be made unless there is an **undue burden** on the Examiner to examine all of the claims in a single invention.

In the instant case, Applicants believe that the fields of search for peptides and peptide derivatives that have binding affinity for VLA-4 are coextensive for antibodies that bind alpha-4 subunit of VLA-4. Since an examination on the merits has already been performed for such antibodies, Applicants submit that a search for the peptides that have the same binding affinity as the antibody would not be overly burdensome. In fact, no showing has been adduced as to why such a search is perceived as burdensome, as required.

Furthermore, claim 22 is directed to treating viral encephalitis comprising administering an agent that inhibits binding of leukocytes to brain endothelial cells via leukocyte surface antigen alpha-4 integrin, wherein said agent comprises peptides of SEQ ID NOS: 3-5. The Examiner has repeatedly indicated that claims directed to methods utilizing the peptides of SEQ ID NOS: 3-5 are enabled. See March 11, 2003 Official Action, Item 4, page 2, lines 29-30, and page 3, lines 27-28; July 29, 2002 Official Action, Item 4, page 3, lines 22-24. Thus, it seems that the Examiner has already contemplated such claims in his examination on the merits. Morever, the Examiner **invited** the Applicants on numerous occasions to specifically recite the particular peptides of SEQ ID NOS: 3-5 in the claims. See March 11, 2003 Official Action, Item 4, page 3, line 30, page 4, lines 25-26; July 29, 2002 Official Action, Item 4, page 3, line 26, page 5, lines 22-23. It is presumptively unfair to withdraw claims as being drawn to non-elected subject matter, when in fact the Examiner invited the Applicants to submit such claims. Thus, in view of the above, Applicants submit that examination of claims directed to SEQ ID NOS: 3-5 would not require any further burden upon the Examiner.

In addition, clarification is requested regarding the status of claim 21. Claims 21-22 are indicated as being withdrawn from consideration. However, non-elected claim 21 is also **included** in the rejection of claims 1-8, 11, 14-18 under 35 U.S.C. § 112, first paragraph. As a consequence, it appears that claim 21 has already been examined on the merits. Accordingly, it would not require any further burden upon the Examiner to continue to examine this claim, and it would be improper to withdraw the claim as being drawn to a non-elected invention.

Thus, for at least the reasons stated above, Applicants respectfully request that the withdrawal of this restriction requirement and that claims 21-22 be examined on the merits.

II. FORMAL MATTERS

A. Drawings

The Examiner has acknowledged that the corrected formal Drawings filed with the Amendment and Reply of December 30, 2002 comply with 37 C.F.R. § 1.84. See March 11, 2003, Official Action, Item 5.

B. Objections and Rejections Withdrawn

The objections to the Drawings and the Specification, and the rejection of claim 19 under 35 U.S.C. § 112, second paragraph, have been withdrawn in view of the Amendment and Reply filed December 30, 2002.

III. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SCOPE OF ENABLEMENT

A. Enablement

Claims 1-8, 11, 14-19 and non-elected claim 21 stand rejected under 35 U.S.C. § 112, first paragraph, because the Specification, while enabling for the treatment of viral encephalitis by administering "antibodies that bind the alpha-4 subunit of VLA-4" and "peptides of SEQ ID NOS: 3-5," purportedly does not provide enablement for "any other agent that inhibits the binding of leukocytes to brain endothelial cells via leukocyte surface antigen alpha-4 integrin." See March 11, 2003 Official Action, Item 4. For at least all of the reasons set forth below, Applicants respectfully traverse this rejection and request its withdrawal.

The Examiner acknowledges that the Specification teaches how to find and screen various agents for the requisite ability to inhibit binding of leukocytes to brain endothelial cells via leukocyte surface antigen alpha-4 integrin. In this regard, the Specification teaches numerous agents includes antibodies and small molecules, peptides that inhibit binding of leukocytes to brain endothelial cells via leukocyte surface antigen alpha-4 integrin. Nonetheless, the Examiner submits that in providing such a description on how

to conduct screening assays, the Specification essentially calls for the use of trial and error. Applicants again respectfully traverse this position. It is well established that a disclosure of every species is not required and that even a single embodiment may provide broad enablement. In the instant case, as the Examiner has admitted, the Specification provides numerous representative examples of the claimed therapeutic agents. These include antibodies that bind the alpha-4 subunit of VLA-4 (Specification, page 9, lines 11-24; page 10, lines 11-20; and page 12, lines 5-29), fragments to such antibodies (Specification, page 13, lines 13-30), and peptides that have the binding affinity for VLA-4 (Specification, page 9, lines 25 to page 10, line 6), also see SEQ ID NOS: 3-5. Based on these examples, the Specification also teaches numerous methods and assays to screen potential therapeutic agents for the appropriate binding specificity and/or the capacity to block the interaction of VLA-4 receptor with inflamed endothelial cells, other cells bearing a VCAM-1 counterreceptor, or purified VCAM-1 counterreceptor. See Specification, page 8, line 12 to page 9, line 8; and page 15, lines 14-31.

Likewise, the Specification also describes extensive teachings as to how to obtain binding agents by producing and screening such agents for their ability to inhibit leukocytes bearing VLA-4 from binding to CNS endothelial cells. See Specification, pages 9-10, page 15, line 14 to page 16, line 4.

The Specification further discloses that the libraries of compounds can be initially screened for specific binding to the alpha-4 integrin subunit of VLA-4 or to VCAM-1, optionally in competition with a reference compound known to have blocking activity. Appropriate activity can then be confirmed using one of the assays described at pages 8 and 9 of the Specification. These methods and assays were well within the purview of one of skill in the art at the time of the claimed invention, and would not require undue experimentation to perform.

Based on the representative examples provided in the Specification, Applicants submit that it would not require undue experimentation to practice the invention as claimed. Thus, for at least these reasons, Applicants respectfully request the withdrawal of this rejection.

B. Incorporation by Reference

The Examiner alleges that Applicants appear to rely upon the disclosure of peptides disclosed in WO 96/22966, WO 96/20216, WO 96/00581, and WO 96/06108, as well as, U.S. Patent No. 5,510,332. See March 11, 2003, Official Action, Item 4.

The Examiner has indicated that the peptides of SEQ ID NOS: 3-5 and the peptides in U.S. Patent No. 5,510,332 are properly disclosed in the current Specification. However, with respect to references incorporated in the instant application that disclose methods for screening additional reagents with the claimed binding characteristics, the Examiner believes that these teachings constitute essential subject matter, and therefore cannot be incorporated by reference.

Applicants respectfully traverse this position. First, the presently claimed invention is not directed to specific agents that inhibit leukocyte binding to endothelial cells. Instead, the claimed invention is directed to the use of such agents in treating viral encephalitis. In this regard, various reagents with the required binding characteristics are made available in the instant Specification. Second, other reagents can be identified by using various routinely practiced high throughput screening methods. Based upon the representative examples disclosed, Applicants submit that the identification of other reagents is well within the purview of one of skill in the art. It is well established that a Specification need not teach, and preferably omits, what is well known in the art. Hybritech, Inc. v. Monoclonal Antibodies, Ind., 802 F.2d 1367, 1368, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986); In re Buchner, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991); and M.P.E.P. § 2164.01. Third, Applicants submit that all of the these reagents are exemplary, rather than essential for the presently claimed invention. Accordingly, Applicants submit that the identity of an agent is not "essential materials" of the subject invention and that one of skill in the art could practice the claimed invention without undue experimentation given the provided examples. Therefore, withdrawal of this rejection is respectfully requested.

In the event that the Examiner decides to maintain this rejection, Applicants invite the Examiner to contact the Applicant and identify the specific subject matter that is deemed to be missing from the instant Specification.

IV. REJECTIONS UNDER 35 U.S.C. § 103(a)

A. Bendig and/or Soilu-Hanninen (1996) and/or Soilu-Hanninen (1997) in view of Ashwell

Claims 1-18 and newly added claim 20 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Bendig *et al.* U.S. Patent No. 5,840,299 ("Bendig") and/or Soilu-Hanninen *et al.*, SCAND. J. IMMUNOL., 43: 727 (1996) ("Soilu-Hanninen (1996)") and/or Soilu-Hanninen *et al.*, J. NEUROIMMUNOL., 72: 95-105 (1997) ("Soilu-Hanninen (1997)") and further in view of Ashwell *et al.* U.S. Patent No. 6,291,453 ("Ashwell"). See March 11, 2003 Official Action, Item 6.

Applicants respectfully traverse this rejection for the reasons previously set forth in the Amendment and Reply dated December 30, 2002, and for the reasons discussed below.

i) Failure to Teach Each and Every Element of the Claimed Invention

The cited prior art fails to render obvious the claimed invention, because the cited references fail teach each and every element of the claimed invention.

It is well established that the prior art references must teach or suggest each and every element of the claimed invention. See M.P.E.P. § 2143.03; In re Royka, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); In re Zurko, 111 F.3d 887, 888-89, 42 U.S.P.Q.2d 1476, 1478 (Fed. Cir. 1997); In re Wilson, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

In this case, the cited references fail to teach a method of treating **viral encephalitis** infected patients that are **free of MS** using agents, which inhibit the binding of leukocytes to brain endothelial cells via the leukocyte cell surface antigen alpha-4 integrin. The Examiner again relies on Ashwell, Bendig, Soilu-Hanninen (1996), and Soilu-Hanninen (1997) as allegedly teaching VLA-4α-specific antibodies to treat encephalitis

(allegedly including herpesvirus-induced encephalitis) **and** MS. However, the combined references fail to teach the treatment of viral encephalitis infected patients that are free of MS.

For instance, Bendig relates to the use of VLA-α4-specific antibodies in the treatment of MS. While Bendig mentions encephalitis, the reference fails to teach a method of treating **viral encephalitis** infected patients that are **free of MS** using agents to inhibit the binding of leukocytes to brain endothelial cells via the leukocyte cell surface antigen alpha-4 integrin. Moreover, as set forth in the references cited by Applicants, the etiologies and pathologies of viral encephalitis and MS are completely different. These differences are such that one skilled in the art would not believe that treatment of one condition would correspondingly (let alone efficaciously) treat the other.

Soilu-Hanninen (1996) merely reports that HSV was present in more MS cases than control ones (i.e., 46% of MS cases and 28% of control cases have HSV-1 or HSV-2). Similarly, Soilu-Hanninen (1997) discusses the treatment of virus-facilitated EAE with VLA-4-specific mAb. In Soilu-Hanninen (1997), the virus used to induce EAE was Semliki Forest virus, which is an alphavirus, and not a herpesvirus as required in the claims. However, unlike the claimed methods, neither Soilu-Hanninen reference proposes treating encephalitis in herpesvirus infected patients that **are free of MS**.

Ashwell discloses 4-amino-phenylalanine type compounds which inhibit leukocyte adhesion mediated by VLA-4. Ashwell indicates that such compounds can be useful for the treatment of MS. Ashwell fails to teach a method of treating **viral encephalitis** infected patients that are **free of MS** using agents to inhibit the binding of leukocytes to brain endothelial cells via the leukocyte cell surface antigen alpha-4 integrin.

Thus, the cited references fail to teach when viewed alone or in combination, a method of treating **viral encephalitis** infected patients that are **free of MS** using agents to inhibit the binding of leukocytes to brain endothelial cells via the leukocyte cell surface antigen alpha-4 integrin. For at least his reason, Applicants respectfully request the withdrawal of this rejection because no *prima facie* case of obviousness has been adduced.

ii) No Suggestion/Motivation To Either Modify or Combine the References' Teachings To Arrive at the Claimed Invention

The cited prior art fails to render obvious the claimed invention, because the references fail to provide at least the requisite suggestion/motivation to either modify and/or combine the reference teachings to arrive at the claimed invention.

It is well established that there must be some suggestion or motivation in the references to either modify or combine the reference teachings to arrive at the claimed invention. See M.P.E.P. § 2143; In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

As discussed above, the cited references fail to teach and/or suggest a method of treating **viral encephalitis** infected patients that are **free of MS**. Accordingly, there is no motivation to modify the claimed invention to arrive at the claimed invention.

Moreover, Applicants previously submitted the following journal articles to highlight the extensive differences between MS and viral encephalitis, and to further illustrate that at the time of the claimed invention, EAE and MS were not predictive for viral encephalitis:

- Sadiq *et al.*, MERRITT'S TEXTBOOK OF NEUROLOGY, Chapter 128: Demyelinating Diseases, pp. 804-29 (Rowland ed., Williams & Wilkins, Baltimore, 1995) ("Sadiq");
- Jubelt *et al.*, MERRITT'S TEXTBOOK OF NEUROLOGY, Section III: Infections of the Nervous System, Chapter 23: Viral Infections, pp. 142-79 (Rowland ed., Williams & Wilkins, Baltimore, 1995) ("Jubelt");
- Gilden, JAMA, 286(24): Editorial (2001) ("Gilden");
- Taus *et al.*, ACTA. NEUROL. SCAND., 101(4):224-8 (2000) ("Taus");
- Martin *et al.*, ACTA NEUROL. SCAND., 95(5):280-3 (1997) ("Martin"); and
- Simmons, HERPES, 8(3):60-3 (2001) ("Simmons").

These references, which were previously submitted with the Amendment and Reply of December 12, 2002, demonstrate that at the time of the claimed invention, the alleged association between viral encephalitis and MS **was controversial** and **inconclusive** at best.

While many viruses and pathogens were allegedly thought to be associated with MS, **none** were linked to the disease. Moreover, these references, and in particular, the Martin reference, specifically investigated the relationship between herpesviruses and MS, and found **no relationship** between herpesviruses and MS. In fact, the results in Martin argued against a continuous disseminated herpesvirus infection in MS.

These references also indicate that MS and viral encephalitis are vastly different disease conditions, both histologically and anatomically. At the time of the claimed invention, the etiologies and pathologies of both were unknown. In fact, at the time of the claimed invention, there was no meaningful similarity between MS to viral encephalitis to suggest that an animal model for one would be a suitable model for the study of or predictive for efficacy in the other disease.

Thus, those skilled in the art at the time of the claimed invention, and still today, would have reasonably believed that MS, as well as the EAE model, are **different** and **distinguishable** from viral encephalitis. Accordingly, no artisan at the time of the claimed invention would have recognized the diseases or their models as correlative. Certainly, the skilled artisan would not have concluded EAE (and thereafter MS) to be analogous to viral encephalitis. As such, EAE models and methods of treatment for MS would not have been predictive for viral encephalitis. Any suggestion otherwise amounts to proceeding with no reasonable expectation of success.

iii) No Reasonable Expectation of Success

The cited prior art references fail to provide a reasonable expectation of success.

It is well established that the prior art must provide a reasonable expectation of success. See M.P.E.P. § 2143.02; Vaeck, 20 U.S.P.Q.2d at 1438; In re Merck & Co., Inc., 231 U.S.P.Q. 375 (Fed. Cir. 1986). Moreover, whether the art is predictable or whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. *Ex parte* Erlich, 3 U.S.P.Q.2d 1011 (Bd. Pat. App. & Inter. 1986).

As discussed above, the prior art references, when viewed in their entirety, clearly demonstrate that there was no clear evidence of a viral component in MS and EAE. As

such, MS and its EAE animal model would not have been correlative and/or predictive for viral encephalitis at the time of the claimed invention. In other words, due to the lack of predictability in the prior art, there was no reasonable expectation of success in combining and/or modifying the references to arrive at the claimed invention.

The Examiner acknowledges that the claimed methods are distinguishable from MS. Nonetheless, the Examiner contends that "[w]hile the claimed methods are distinguished from MS, it **appears** that the combined teachings are consistent with the role of T cells in viral inflammation encompassing viral encephalitis." See March 11, 2003 Office Action, Item 6 [emphasis added]. The Examiner further asserts that there was sufficient motivation and expectation of success based on the role of T cells in viral inflammation encompassing viral encephalitis, via the blocking of VLA-4:VCAM-1 interactions. See March 11, 2003 Office Action, Item 6.

However, the Examiner has failed to provide evidence to support such **conclusory** assertions. As stated above, the only references cited relate to the treatment of MS. From this the Examiner, makes a leap from MS to viral encephalitis. However, this contradicts what was generally known in the art at the time of the claimed invention with regard to EAE, MS, and viral encephalitis, especially in view of the references submitted by the Applicant.

As disclosed throughout the Specification and as discussed above, EAE is an experimentally induced and reproducible syndrome that simulates MS and is **different** from viral encephalitis. See Specification, page 18, lines 9-12. Unlike viral encephalitis, which is caused by an inflammatory response to a systemic viral infection, MS is a complex autoimmune disease of multi-factorial origin. In this regard, the Specification at page 18, lines 13-14, clearly states that "the present methods are **not** employed on EAE models, or humans suffering from MS."

Furthermore, as discussed above, the art at the time of the claimed invention was such that one skilled in the art would not find a credible link between MS and herpesvirus infection. Accordingly, neither EAE nor MS can be said to be predictive models of viral encephalitis. One of ordinary skill in the art at the time of the claimed invention and yet

today would have reasonably believed that EAE and MS are **different** and **distinguishable** from viral encephalitis. As such, EAE models and methods of treatment for MS cannot be said to have been predictive for viral encephalitis.

The Examiner relies on Planz, Sanders, and the Editorial as allegedly countering the argument on lack of predictability. However, these references are inapplicable to the instant rejection since they were not cited as prior art. These references were only cited in the second obviousness rejection. It is apparent that the Examiner has argued both obviousness rejections together. Nonetheless, these references fail to remedy deficiencies noted in the other prior art references. As discussed above, Gilden, Taus, Martin, and Simmons clearly teach that there is no link between herpesvirus and MS. Thus, MS and its animal model, EAE, cannot then be said to be predictive of viral induced encephalitis (*i.e.*, immune-induced inflammation).

At best, the Examiner's assertion that ". . . it **appears** that the combined teachings are consistent with the role of T cells in viral inflammation encompassing viral encephalitis" is a clear indication that the rejection employs an improper "obvious to try" rationale at best.

It is well established that in moving from the prior art to the claimed invention, one cannot base a determination of obviousness on what one of ordinary skill in the art might try or find obvious to try. In re O'Farrel, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988). Indeed, the proper test requires determining what the prior art would have led the skilled artisan to do.

The Examiner attempts to counter this argument by asserting that the ultimate conclusion of law regarding the determination of obviousness may at times properly be drawn from an inference of fact arising prior art teachings. Nonetheless, the proper legal test requires determining what the prior art would have led the skilled artisan to do, not what would have been obvious to try.

Moreover, it is well established that a prior art teaching must be considered as a whole including portions that "teach away" from the claimed invention. See M.P.E.P. § 2141.02; W.L. Gore & Associates, Inc., v. Garlock, Inc., 220 U.S.P.Q. 303 (Fed. Cir.

1983), cert. denied, 469 U.S. 851 (1984). Similarly, references cannot be combined where the references teach away from their combination. M.P.E.P. § 2145; In re Grasselli, 218 U.S.P.Q. 769, 779 (Fed. Cir. 1983). The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of non-obviousness. M.P.E.P. § 2145; In re Hedges, 228 U.S.P.Q. 685 (Fed. Cir. 1986).

In this case, the clear inference drawn from the totality of the prior art and what was known in the art at the time of the claimed invention, clearly teaches away from the claimed invention. Based on the general state of the art at the time of the claimed invention as demonstrated in the references provided, there was no meaningful correlation between MS and viral encephalitis.

Moreover, assuming *arguendo* that the cited art disclosed the ability of certain agents to block undesired inflammation in non-viral encephalitis, one skilled in the art would **not** be motivated to use these agents to treat virus induced encephalitis for fear of eliminating the desired aspects of an inflammatory response in clearing viral infection. It is well understood that inflammatory responses are desirable in clearing viral infection. In this regard, the Specification at page 4, line 28 to page 5, line 15, teaches that BDV-specific CF4+ T-cells can both ameliorate and augment Borna virus infection. For instance, when administered to an experimental animal before infection, the cells are protective, however, when administered after infection, they augment the symptoms of disease. Thus, those skilled in the art would not be motivated to use agents that block the inflammatory response to treat a viral infection. By contrast, the claimed invention solves this problem in the art by effectively suppressing the harmful effects of virus induced inflammation without significantly suppressing the beneficial effects of inflammation that inhibit viral replication.

Thus, in view of the above, the claimed invention is not obvious over the cited references because the cited art references fail to teach each and every element of the claimed invention, lack a suggestion to combine/modify the reference teachings to arrive at the claimed invention and do not contain a reasonable expectation of success at arriving at the claimed invention. Therefore, Applicants respectfully request the withdrawal of this rejection.

B. Bendig and/or Soilu-Hanninen (1996) and/or Soilu-Hanninen (1997) in view of Ashwell and in view of Planz and/or Sanders and/or Editorial

Claims 1-18 and 20 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Bendig *et al.* U.S. Patent No. 5,840,299 ("Bendig") and/or Soilu-Hanninen *et al.*, SCAND. J. IMMUNOL., 43:727 (1996) ("Soilu-Hanninen (1996)") and/or Soilu-Hanninen *et al.*, J. NEUROIMMUNOL., 72:95-105 (1997) ("Soilu-Hanninen (1997)") and further in view of Ashwell *et al.*, U.S. Patent No. 6,291,453 ("Ashwell"), and further in view of the art known role or etiology of various viruses including encephalitis, as evidenced by Planz *et al.*, J. VIROL., 68:896-903 (1995) ("Planz") and/or the role of herpesviruses in MS as evidenced by Sanders *et al.*, ARCHIVES OF NEUROLOGY, 53:125-133 (1996) ("Sanders 1") and/or Editorial, ARCHIVES OF NEUROLOGY, 53:123-124 (1996) ("Sanders 2"). See March 11, 2003 Office Action, Item 6.

Applicants respectfully traverse this rejection for the same reasons noted above. Bendig, Soilu-Hanninen (1996), Soilu-Hanninen (1997), and Ashwell fail for the reasons discussed above. The secondary references do not cure the defects inherent to the primary references and do not teach the claimed invention when viewed alone.

The Examiner relies on Planz, Sanders, and the Editorial as allegedly providing the requisite motivation to apply the claimed treatment to patients with viral encephalitis, in particular, to patients herpesvirus induced viral encephalitis. However, as discussed above, Gilden, Taus, Martin, and Simmons clearly teach that there is no link between herpesvirus and MS. Thus, MS and its animal model, EAE, cannot then be said to be predictive of viral induced encephalitis (i.e., immune-induced inflammation). One of ordinary skill in the art at the time of the claimed invention would have reasonably believed that EAE and MS are **different** and **distinguishable** from viral encephalitis. As such, EAE models and methods of treatment for MS cannot be said to have been predictive for viral encephalitis. Thus, Applicants respectfully request the withdrawal of this rejection.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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